

U.S. Patent Application No. 10/681,352  
Amendment dated September 26, 2005  
Response to Office Action dated July 1, 2005

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

1. (Currently amended) A screening method to determine effective cancer curative treatment medicines, comprising:
  - (1) determining position(s) at least one position of at least one polymorphic amino acid(s) acid in at least one amino acids sequence(s) acid sequence, including encoded by at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA,
  - (2) analyzing variations of the polymorphic position(s) at least one position of the at least one polymorphic amino-acid(s) acid, and survival results (prognosis, treatment effects) in a patient population by one of the following cancer treatments: {the cancer resection alone with (no adjuvant therapy), the anticancer chemotherapy after the cancer resection (Chemotherapy), or and the anticancer immunotherapy after the cancer resection (Immunotherapy)},
  - (3) determining positions of the amino acids and the amino acid(s), which have been estimated to variations of the at least one position of the at least one polymorphic amino acid that have a statistically significant relationship with at least one of the treatments,
  - (4) creating a three-dimensional structure of at least one amino acid sequences including the amino acids sequence encoded by at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA and containing at least one variation determined in step (3), and
  - (5) using the interactions of candidate compounds with the three-dimensional structure

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as a marker screening a set of candidate compounds to determine candidate compounds  
that interact with the three-dimensional structure, wherein candidate compounds that  
interact with the three-dimensional structure are identified as cancer treatment medicines.

2. (Original) The method according to claim 1, wherein cancer is analyzed by distinguishing stomach cancer and others.
3. (Original) The method according to claim 1, which is carried out by utilizing drug designing techniques based on comparison with the three-dimensional structure of the candidate compounds.
4. (Currently amended) The method according to claim 1, wherein effective cancer curative treatment medicines can suppress and control metastasis of cancer.
5. (Currently amended) The method according to claim 1, wherein effective cancer curative treatment medicines are immunological medicines.
6. (Currently amended) The method according to claim 1, wherein effective cancer curative treatment medicines are chemotherapeutic medicines.
7. (Currently amended) The method according to claim 1, wherein the effectiveness of the cancer curative treatment medicines is measured by:
  - (1) contacting the candidate compounds and the three-dimensional structure by alignment and variation of each amino acid under a condition in which the-an interaction between the candidate compounds and the three-dimensional structure is possible,
  - (2) evaluating the interaction of the three-dimensional structure with the candidate compounds , and detecting a signal of the interaction.
8. (Original) The method according to claim 7, wherein cancer is analyzed by distinguishing stomach cancer and other cancers.

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9. (Original) The method according to claim 1, wherein both effectiveness of the anticancer treatments and the variations of the base sequences coding the polymorphic amino acids on any one of DRB1\*gene, DQB1\*gene, and DPB1\* gene of HLA, are analyzed.
10. (Original) The method according to claim 7, wherein both effectiveness of the anticancer treatments and the variations of the base sequences coding the polymorphic amino acids on any one of DRB1\*gene, DQB1\*gene, and DPB1\* gene of HLA, are analyzed.
11. (Currently amended) A measuring method for evaluating anticancer treatments, comprising:
  - (1) determining position(s) at least one position of at least one polymorphic amino acid(s) acid in at least one amino acids sequence(s) acid sequence, including encoded by at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA,
  - (2) analyzing variations of the polymorphic position(s) at least one position of the at least one polymorphic amino-acid(s) acid, and survival results (prognosis, treatment effects) in a patient population by one of the following cancer treatments: [the cancer resection alone with (no adjuvant therapy), the anticancer chemotherapy after the cancer resection (Chemotherapy), or the anticancer immunotherapy after the cancer resection (Immunotherapy)],
  - (3) determining positions of the amino acids and the amino acids, which have been estimated to variations of the at least one position of the at least one polymorphic amino acid that have a statistically significant relationship with at least one of the treatments, and
  - (4) utilizing the specified positions and the corresponding amino acid(s) as a marker determining an amino acid sequence encoded by at least one of DRB1\*gene,

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DQB1\*gene, and DPB1\*gene of HLA of a patient and determining whether amino acids at polymorphic positions encoded by at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA of the patient correlates with a variation determined in step (3) to have a statistically significant relationship with at least one of the cancer treatments.

12. (Original) The method of claim 11, wherein cancer is analyzed by distinguishing stomach cancer from other cancers.
13. (Currently amended) A measuring method for evaluating cancer treatments, comprising:
  - (1) determining position(s) at least one position of at least one polymorphic amino acid(s) acid in at least one amino acid acids sequence(s) sequence, including encoded by at least one of, DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA,
  - (2) analyzing variations of the base sequences coding the polymorphic positions at least one position of the at least one polymorphic amino acid, and survival results (prognosis, treatment effects) in a patient population by one of the following cancer treatments: [the cancer resection alone with (no adjuvant therapy), the anticancer chemotherapy after the cancer resection (Chemotherapy), the or anticancer immunotherapy after the cancer resection (Immunotherapy)],
  - (3) determining position(s) of the amino acids and the amino acid(s) which have been estimated to variations of the base sequences coding at least one of the polymorphic amino acid that have a statistically significant relationship with the treatments, and the corresponding base sequences, and
  - (4) utilizing the specified positions and the amino acids together with the corresponding base sequences as a marker determining a base sequence of at least one of

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DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA of a patient and determining whether base sequences of polymorphic positions of at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA of a patient correlates with a variation determined in step (3) to have a statistically significant relationship with at least one of the cancer treatments.

14. (Original) The method according to claim 13, wherein cancer is analyzed by distinguishing stomach cancer from other cancers.

15. - 18. (Canceled)

19. (New) A composition comprising an isolated polypeptide having an amino acid sequence encoded by least one of a polymorphic variation of a DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA, wherein the identity and/or position of the amino acids of the polymorphic variation has a statistically significant relationship with a cancer treatment.

20. (New) The composition of claim 19 wherein the amino acid sequence is selected by

(1) determining at least one position of at least one polymorphic amino acid in at least one amino acid sequence encoded by at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA,

(2) analyzing variations of the at least one position of the at least one polymorphic amino acid and survival results in a patient population by one or more of the following cancer treatments: cancer resection alone with no adjuvant therapy, anticancer chemotherapy after the cancer resection, or anticancer immunotherapy after the cancer resection, and

(3) determining variations of the at least one position of the at least one polymorphic amino acid that have a statistically significant relationship with at least one of the cancer treatments.

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21. (New) The composition according to claim 19, wherein cancer is analyzed by distinguishing stomach cancer from other cancers.
22. (New) A composition comprising an isolated polypeptide encoding a polymorphic variation of a DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA, wherein the polymorphic variation has a statistically significant relationship with a cancer treatment.
23. (New) The composition of claim 22 wherein the amino acid sequence is selected by
  - (1) determining at least one position of at least one polymorphic amino acid in at least one amino acid sequence encoded by at least one of DRB1\*gene, DQB1\*gene, and DPB1\*gene of HLA,
  - (2) analyzing variations of base sequences coding at least one of the at least one polymorphic amino acid, and survival results in a patient population by one or more of the following cancer treatments: cancer resection alone with no adjuvant therapy, anticancer chemotherapy after cancer resection, or anticancer immunotherapy after cancer resection, and
  - (3) determining variations of the base sequences coding at least one of the polymorphic amino acid that have a statistically significant relationship with at least one of the cancer treatments.
24. (New) The method according to claim 23, wherein cancer is analyzed by distinguishing stomach cancer from other cancers.